

Atty. Dkt. No. 041673-2092

Amendments to the Claims:

Please cancel claims 1, 7, 15 and 22. Please amend claims 2 through 6, 8 through 14, 16, 18 through 21, 23 through 32, 37, 42 through 44, and 47 through 51. Please add claims 52 through 64. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Cancelled).
2. (Presently Amended) ~~An isolated polynucleotide sequence~~ A nucleic acid molecule encoding a chimeric TNFa ligand polypeptide, comprising a first polynucleotide nucleotide sequence encoding a domain III or a subdomain of domain III of a tumor necrosis factor ligand other than TNFa, wherein the Domain III fragment of a tumor necrosis factor ligand other than TNFa lacking a metalloproteinase cleavage site ~~encoded domain or subdomain~~ replaces a cleavage site of native TNFa, and a second polynucleotide nucleotide sequence encoding a Domain IV domain fragment or subdomain of native TNFa protein that binds to a human TNFa receptor.
3. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claim 1 or claim 2 ~~wherein the first nucleotide sequence additionally~~ further comprising a third polynucleotide that encodes Domain domain II, or a subdomain of domain II, II fragment of the other tumor necrosis factor ligand.
4. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claims 1, 2 or 3, ~~wherein the first nucleotide sequence additionally~~ further comprising a fourth polynucleotide that encodes a Domain domain I, or a subdomain of domain I, I fragment of the other tumor necrosis factor ligand.
5. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claims 1, 2, 3 or 4 wherein the first polynucleotide nucleotide sequence additionally further encodes a subdomain of domain Domain IV fragment of the other tumor necrosis factor ligand.
6. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence claim 1 ~~or of~~ claim 2, wherein the other tumor necrosis factor ligand is selected from the group consisting of CD154, CD70, Fas ligand, NGE, CD30, TNF β , 4-1BBL and TRAIL. ~~CD154, CD70, Fas ligand and TRAIL.~~
7. (Cancelled).

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8. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claim 7 ~~2~~, wherein the second polynucleotide nucleotide sequence encodes a Domain subdomain of domain IV fragment of native TNFa that lacks a cleavage site of native TNFa protein.

9. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claim 1 or claim 2 wherein the first polynucleotide further nucleotide sequence encodes domains Domain I, II or III fragments, or subdomains of one or more of domains 1, II and III, of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand, NGF, TNF β , CD30, 4-1BBL and TRAIL, and the second polynucleotide nucleotide sequence encodes domain IV, or a subdomain of domain Domain IV, of native TNFa protein.

10. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claim 9 wherein the first nucleotide sequence polynucleotide further nucleotide sequence encodes domains Domain I, II or III fragments of CD154 protein, and the second nucleotide sequence encodes domain IV, or a subdomain of domain IV, of native TNFa.

11. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claim 1 or claim 2 further comprising a wherein the sequence additionally includes a linker domain encoding a peptide of at least one amino acid that links the first polynucleotide nucleotide sequence to the second polynucleotide nucleotide sequence.

12. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claim 1 or claim 2, comprising a polynucleotide wherein the sequence is selected from the group consisting of SEQ.ID. NO. 1, SEQ.ID. NO. 2, SEQ.ID. NO. 3 and SEQ.ID. NO. 4.

13. (Presently Amended) The nucleic acid molecule isolated polynucleotide sequence of claim 1 or claim 2, wherein the chimeric TNFa polypeptide comprises an amino acid sequence selected from the group consisting of SEQ.ID. NO. 5, SEQ.ID. NO. 6, SEQ.ID. NO. 7 and SEQ.ID. NO. 8.

14. (Presently Amended) A chimeric TNFa, comprising a first Domain III domain fragment or subdomain of a tumor necrosis factor ligand other than TNFa lacking a matrix metalloproteinase, wherein the domain fragment or subdomain replaces a cleavage site of native TNFa, and a second Domain IV domain fragment or subdomain of native TNFa that binds to a TNFa receptor.

15. (Cancelled).

16. (Presently Amended) The chimeric TNFa of claim 14 or claim 15 that is less susceptible to cleavage from the surface of cells than native TNFa.

17. (Original) The chimeric TNFa of claim 16, wherein the cleavage rate of the chimeric

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TNF α is at least 90% less than that of native TNF α .

18. (Presently Amended) The chimeric TNF α of claim 14 ~~or claim 15, wherein the domain or subdomain further comprising comprises a Domain domain II, or a subdomain of domain II, II fragment~~ of the other tumor necrosis factor ligand.

19. (Presently Amended) The chimeric TNF α of claims 14, ~~15~~ or 18, ~~wherein the domain or subdomain further comprising comprises a Domain domain I, or a subdomain of domain I, I fragment~~ of the other tumor necrosis factor ligand.

20. (Presently Amended) The chimeric TNF α of claims 14, ~~15~~ 18 or 19, ~~wherein the domain or subdomain further comprises comprising a fourth Domain IV fragment a subdomain of domain IV of the other tumor necrosis factor ligand.~~

21. (Presently Amended) The chimeric TNF α of claim 14 ~~or claim 15, wherein the other tumor necrosis factor ligand is selected from the group consisting of CD154, CD70, Fas ligand and TRAIL. CD154, CD70, Fas ligand, NGF, CD30, TNF β , 4-1BBL and TRAIL.~~

22. (Cancelled).

23. (Presently Amended) The chimeric TNF α of claim 14, ~~wherein the 22 comprising a Domain IV fragment subdomain of domain IV of native TNF α that lacks a cleavage site of native TNF α protein.~~

24. (Presently Amended) The chimeric TNF α of claim 14 ~~or claim 15, comprising domains I, II and III, or subdomains of one or more of domains I, II and III, of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand, NGF, CD30, TNF β , 4-1BBL and TRAIL. CD154, CD70, Fas ligand and TRAIL, and domain IV, or a subdomain of domain IV, of native TNF α protein.~~

25. (Presently Amended) The chimeric TNF α of claim ~~wherein 14 or claim 15, comprising domain I, domain II and domain III, or subdomains of one or more of the domains I, II and III are~~ of CD154 ~~protein, and domain IV, of a subdomain of domain IV, of native TNF α .~~

26. (Presently Amended) The chimeric TNF α of claim 14, ~~further or claim 15 additionally comprising a linker domain encoding a peptide of at least one amino acid that links the Domain III first domain fragment or subdomain to the Domain IV second domain fragment or subdomain.~~

27. (Presently Amended) An expression vector, comprising the nucleic acid molecule isolated polynucleotide sequence of claim 2 ~~1~~.

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28. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 3. ~~The expression vector of claim 27, wherein the polynucleotide sequence encodes a chimeric TNF α comprising domain 111, or a subdomain of domain III, of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand and TRAIL, and domain IV, or a subdomain of domain IV, of native TNF α .~~

29. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 4. ~~The expression vector of claim 28, further comprising a polynucleotide sequence that encodes domain 11, or a subdomain of domain 11, of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand and TRAIL.~~

30. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 9. ~~The expression vector of claim 28 or claim 29, further comprising a polynucleotide sequence that encodes domain 1, or a subdomain of domain 1, of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand and TRAIL.~~

31. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 11. ~~The expression vector of claim 28 or claim 29, further comprising a polynucleotide sequence that encodes a subdomain of domain IV of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand and TRAIL.~~

32. (Presently Amended) The expression vector of claim 27 28, further comprising viral DNA or bacterial DNA.

33. (Original) The expression vector of claim 32 wherein said viral DNA is selected from the group consisting of adenoviral DNA or retroviral DNA.

34. (Original) The expression vector of claim 32, wherein at least a portion of the vector comprises adenoviral DNA.

35. (Original) The expression vector of claim 27, further comprising a promoter region.

36. (Original) The expression vector of claim 27, further comprising a polyadenylation signal region.

37. (Presently Amended) A genetic construct comprising the nucleic acid molecule ~~isolated polynucleotide sequence~~ according to ~~claim 1 or~~ claim 2 operatively linked to a promoter sequence and to a polyadenylation signal sequence.

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38. (Original) A host cell, comprising an expression vector according to claim 27 or a genetic construct according to claim 37.
39. (Original) The host cell of claim 38, wherein the cell is a mammalian cell.
40. (Original) The host cell of claim 39 ; wherein the cell is a tumor cell.
41. (Original) The host cell of claim 39, wherein the cell is an antigen presenting cell.
42. (Presently Amended) A process for producing a chimeric TNFa of claim 14 ~~or claim 15~~ comprising culturing a host cell of claim 38 under conditions suitable to effect expression of the protein.
43. (Presently Amended) A method for increasing the concentration of a ligand capable of binding to a TNFa receptor on the surface of a cell, comprising introducing into the cell a nucleic acid molecule ~~an isolated polynucleotide sequence~~ encoding a chimeric TNFa polypeptide according to ~~claim 1 or~~ claim 2, whereby the chimeric TNFa polypeptide is less susceptible to cleavage from the surface of the cells than a ~~native~~ TNFa protein.
44. (Presently Amended) The method of claim 43, wherein the ~~isolated polynucleotide sequence~~ comprises an expression vector according to claim 27 or a genetic construct according to claim 37.
45. (Original) The method of claim 44 wherein the cell is a mammalian cell.
46. (Original) The method of claim 44 wherein the cell expresses a TNFa receptor on its surface.
47. (Presently Amended) A method for inducing apoptosis of a cell expressing a TNFa receptor, comprising introducing into the cell an ~~isolated polynucleotide sequence~~ encoding a chimeric TNFa polypeptide according to claim 1 or claim 2 wherein the chimeric TNFa is expressed on the surface of the cell.
48. (Presently Amended) A method for inducing activation of an immune system cell, comprising introducing into the cell a nucleic acid molecule ~~an isolated polynucleotide sequence~~ encoding a chimeric TNFa polypeptide according to ~~claim 1 or~~ claim 2 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
49. (Presently Amended) A method for treating neoplasia in a patient comprising introducing into a neoplastic cell a nucleic acid molecule ~~an isolated polynucleotide sequence~~ encoding a chimeric TNFa polypeptide according to ~~claim 1 or~~ claim 2 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.

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50. (Presently Amended) The method of claim 49 further comprising: obtaining the neoplastic cell from a human patient; infusing the neoplastic cell back into the patient after having introduced into the cells the nucleic acid molecule ~~polynucleotide sequence~~ encoding the chimeric TNFa polypeptide.

51. (Presently Amended) A method of treating neoplasia comprising directly injecting into a tumor bed of a patient the nucleic acid molecule ~~an isolated polynucleotide sequence~~ encoding a chimeric TNFa polypeptide according to ~~claim 1~~ or claim 2 wherein the chimeric TNFa polypeptide is expressed in the tumor bed.

52. (New) A nucleic acid molecule encoding a chimeric TNFa ligand polypeptide, comprising a first polynucleotide encoding a Domain III fragment of a tumor necrosis factor ligand other than TNFa, wherein the encoded fragment is a homolog of a cleavage site of native TNFa, and a second polynucleotide encoding a Domain IV fragment of TNFa protein that binds to a TNFa receptor.

53. (New) The nucleic acid molecule of claim 52, further comprising a third polynucleotide that encodes Domain II domain fragment of the other tumor necrosis factor ligand.

54. (New) The nucleic acid molecule of claim 52, further comprising a third polynucleotide that encodes Domain II domain fragment of the other tumor necrosis factor ligand and a fourth polynucleotide that encodes a Domain I domain fragment of the other tumor necrosis factor ligand.

55. (New) The nucleic acid molecule of claim 52, wherein the first polynucleotide further encodes a Domain IV domain fragment of the other tumor necrosis factor ligand.

56. (New) The nucleic acid molecule of claim 52, wherein the other tumor necrosis factor ligand is selected from the group consisting of CD154, CD70, Fas ligand, NGF, CD30, TNF β , 4-1BBL and TRAIL.

57. (New) The nucleic acid molecule of claim 52, comprising a polynucleotide sequence selected from the group consisting of SEQ.ID. NO. 2, SEQ.ID. NO. 3 and SEQ. ID. NO. 4.

58. (New) The nucleic acid molecule of claim 52, encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ. ID. NO. 6, SEQ.ID. NO. 7 and SEQ.ID. NO. 8.

59. (New) An expression vector containing the nucleic acid molecule of claim 52.

60. (New) A host cell containing the nucleic acid molecule of claim 52.

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61. (New) A genetic construct containing the nucleic acid molecule of claim 52.
62. (New) A chimeric TNFa ligand polypeptide, comprising a Domain III fragment of a tumor necrosis factor ligand other than TNFa, wherein the fragment is a homolog of a cleavage site of native TNFa, and a Domain IV fragment of TNFa protein that binds to a TNFa receptor.
63. (New) A method for inducing apoptosis of a cell expressing a TNFa receptor, comprising introducing into the cell an encoding a chimeric TNFa polypeptide according to claim 52 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
64. (New) A method for inducing activation of an immune system cell, comprising introducing into the cell a nucleic acid molecule encoding a chimeric TNFa polypeptide according to claim 52 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
65. (New) A method for treating neoplasia in a patient comprising introducing into a neoplastic cell a nucleic acid molecule encoding a chimeric TNFa polypeptide according to claim 52 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
66. (New) The method of claim 65 further comprising: obtaining the neoplastic cell from a human patient; infusing the neoplastic cell back into the patient after having introduced into the cells the nucleic acid molecule encoding the chimeric TNFa polypeptide.
67. (New) A method of treating neoplasia comprising directly injecting into a tumor bed of a patient the nucleic acid molecule encoding a chimeric TNFa according to claim 52 wherein the chimeric TNFa polypeptide is expressed in the tumor bed.

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Clean Claims As Amended

1. (Cancelled).
2. (Presently Amended) A nucleic acid molecule encoding a chimeric TNFa ligand polypeptide, comprising a first polynucleotide encoding a Domain III fragment of a tumor necrosis factor ligand other than TNFa lacking a metalloproteinase cleavage site and a second polynucleotide encoding a Domain IV fragment of TNFa protein that binds to a TNFa receptor.
3. (Presently Amended) The nucleic acid molecule of claim 2 further comprising a third polynucleotide that encodes Domain II fragment of the other tumor necrosis factor ligand.
4. (Presently Amended) The nucleic acid molecule of claims 2 or 3, further comprising a fourth polynucleotide that encodes a Domain I fragment of the other tumor necrosis factor ligand.
5. (Presently Amended) The nucleic acid molecule of claims 2, 3 or 4 wherein the first polynucleotide further encodes a Domain IV fragment of the other tumor necrosis factor ligand.
6. (Presently Amended) The nucleic acid molecule of claim 2, wherein the other tumor necrosis factor ligand is selected from the group consisting of CD154, CD70, Fas ligand, NGF, CD30, TNF β , 4-1BBL and TRAIL.
7. (Cancelled).
8. (Presently Amended) The nucleic acid molecule of claim 2, wherein the second polynucleotide encodes a Domain IV fragment of native TNFa that lacks a cleavage site of TNFa protein.
9. (Presently Amended) The nucleic acid molecule of claim 2, wherein the first polynucleotide further encodes Domain I, II or III fragments of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand, NGF, TNF β , CD30, 4-1BBL and TRAIL, and the second polynucleotide encodes Domain IV of TNFa protein.
10. (Presently Amended) The nucleic acid molecule of claim 9 wherein the first polynucleotide further encodes Domain I, II or III fragments of CD154 protein.
11. (Presently Amended) The nucleic acid molecule of claim 2 further comprising a linker domain encoding a peptide of at least one amino acid that links the first polynucleotide to the second polynucleotide.

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12. (Presently Amended) The nucleic acid molecule of claim 2, comprising a nucleotide sequence is selected from the group consisting of SEQ.ID. NO. 1, SEQ.ID. NO. 2, SEQ.ID. NO. 3 and SEQ. ID. NO. 4.
13. (Presently Amended) The nucleic acid molecule of claim 2, wherein the chimeric TNFa comprises an amino acid sequence selected from the group consisting of SEQ.ID. NO. 5, SEQ. ID. NO. 6, SEQ.ID. NO. 7 and SEQ.ID. NO. 8.
14. (Presently Amended) A chimeric TNFa, comprising a Domain III fragment of a tumor necrosis factor ligand other than TNFa lacking a matrix metalloproteinase cleavage site and a Domain IV fragment of TNFa that binds to a TNFa receptor.
15. (Cancelled).
16. (Presently Amended) The chimeric TNFa of claim 14 that is less susceptible to cleavage from the surface of cells than native TNFa.
17. (Original) The chimeric TNFa of claim 16, wherein the cleavage rate of the chimeric TNFa is at least 90% less than that of native TNFa.
18. (Presently Amended) The chimeric TNFa of claim 14, further comprising a Domain II fragment of the other tumor necrosis factor ligand.
19. (Presently Amended) The chimeric TNFa of claims 14 or 18, further comprising a Domain I fragment of the other tumor necrosis factor ligand.
20. (Presently Amended) The chimeric TNFa of claims 14, 18 or 19, further comprising a fourth Domain IV fragment of the other tumor necrosis factor ligand.
21. (Presently Amended) The chimeric TNFa of claim 14, wherein the other tumor necrosis factor ligand is selected from the group consisting of CD154, CD70, Fas ligand, NGF, CD30, TNF β , 4-1BBL and TRAIL.
22. (Cancelled).
23. (Presently Amended) The chimeric TNFa of claim 14, wherein the Domain IV fragment lacks a cleavage site of TNFa protein.
24. (Presently Amended) The chimeric TNFa of claim 14, comprising domains I, II and III, of a tumor necrosis factor ligand selected from the group consisting of CD154, CD70, Fas ligand, NGF, CD30, TNF β , 4-1BBL and TRAIL, and domain IV of TNFa protein.

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25. (Presently Amended) The chimeric TNFa of claim wherein one or more of the domains I, II and III are of CD154 protein.
26. (Presently Amended) The chimeric TNFa of claim 14, further comprising a linker domain encoding a peptide of at least one amino acid that links the Domain III fragment to the Domain IV fragment.
27. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 2.
28. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 3.
29. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 4.
30. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 9.
31. (Presently Amended) An expression vector, comprising the nucleic acid molecule of claim 11.
32. (Presently Amended) The expression vector of claim 27, further comprising viral DNA or bacterial DNA.
33. (Original) The expression vector of claim 32 wherein said viral DNA is selected from the group consisting of adenoviral DNA or retroviral DNA.
34. (Original) The expression vector of claim 32, wherein at least a portion of the vector comprises adenoviral DNA.
35. (Original) The expression vector of claim 27, further comprising a promoter region.
36. (Original) The expression vector of claim 27, further comprising a polyadenylation signal region.
37. (Presently Amended) A genetic construct comprising the nucleic acid molecule according to claim 2 operatively linked to a promoter sequence and to a polyadenylation signal sequence.
38. (Original) A host cell, comprising an expression vector according to claim 27 or a genetic construct according to claim 37.

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39. (Original) The host cell of claim 38, wherein the cell is a mammalian cell.
40. (Original) The host cell of claim 39 ; wherein the cell is a tumor cell.
41. (Original) The host cell of claim 39, wherein the cell is an antigen presenting cell.
42. (Presently Amended) A process for producing a chimeric TNFa of claim 14 comprising culturing a host cell of claim 38 under conditions suitable to effect expression of the protein.
43. (Presently Amended) A method for increasing the concentration of a ligand capable of binding to a TNFa receptor on the surface of a cell, comprising introducing into the cell a nucleic acid molecule encoding a chimeric TNFa polypeptide according to claim 2, whereby the chimeric TNFa polypeptide is less susceptible to cleavage from the surface of the cells than a TNFa protein.
44. (Presently Amended) The method of claim 43, wherein the comprises an expression vector according to claim 27 or a genetic construct according to claim 37.
45. (Original) The method of claim 44 wherein the cell is a mammalian cell.
46. (Original) The method of claim 44 wherein the cell expresses a TNFa receptor on its surface.
47. (Presently Amended) A method for inducing apoptosis of a cell expressing a TNFa receptor, comprising introducing into the cell an encoding a chimeric TNFa polypeptide according to claim 1 or claim 2 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
48. (Presently Amended) A method for inducing activation of an immune system cell, comprising introducing into the cell a nucleic acid molecule encoding a chimeric TNFa polypeptide according to claim 2 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
49. (Presently Amended) A method for treating neoplasia in a patient comprising introducing into a neoplastic cell a nucleic acid molecule encoding a chimeric TNFa polypeptide according to claim 2 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
50. (Presently Amended) The method of claim 49 further comprising: obtaining the neoplastic cell from a human patient; infusing the neoplastic cell back into the patient after having introduced into the cells the nucleic acid molecule encoding the chimeric TNFa polypeptide.

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51. (Presently Amended) A method of treating neoplasia comprising directly injecting into a tumor bed of a patient the nucleic acid molecule encoding a chimeric TNF α polypeptide according to claim 2 wherein the chimeric TNF α polypeptide is expressed in the tumor bed.

52. (New) A nucleic acid molecule encoding a chimeric TNF α ligand polypeptide, comprising a first polynucleotide encoding a Domain III fragment of a tumor necrosis factor ligand other than TNF α , wherein the encoded fragment is a homolog of a cleavage site of native TNF α , and a second polynucleotide encoding a Domain IV fragment of TNF α protein that binds to a TNF α receptor.

53. (New) The nucleic acid molecule of claim 52, further comprising a third polynucleotide that encodes Domain II domain fragment of the other tumor necrosis factor ligand.

54. (New) The nucleic acid molecule of claim 52, further comprising a third polynucleotide that encodes Domain II domain fragment of the other tumor necrosis factor ligand and a fourth polynucleotide that encodes a Domain I domain fragment of the other tumor necrosis factor ligand.

55. (New) The nucleic acid molecule of claim 52, wherein the first polynucleotide further encodes a Domain IV domain fragment of the other tumor necrosis factor ligand.

56. (New) The nucleic acid molecule of claim 52, wherein the other tumor necrosis factor ligand is selected from the group consisting of CD154, CD70, Fas ligand, NGF, CD30, TNF β , 4-1BBL and TRAIL.

57. (New) The nucleic acid molecule of claim 52, comprising a polynucleotide sequence selected from the group consisting of SEQ.ID. NO. 2, SEQ.ID. NO. 3 and SEQ. ID. NO. 4.

58. (New) The nucleic acid molecule of claim 52, encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ. ID. NO. 6, SEQ.ID. NO. 7 and SEQ.ID. NO. 8.

59. (New) An expression vector containing the nucleic acid molecule of claim 52.

60. (New) A host cell containing the nucleic acid molecule of claim 52.

61. (New) A genetic construct containing the nucleic acid molecule of claim 52.

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62. (New) A chimeric TNF α ligand polypeptide, comprising a Domain III fragment of a tumor necrosis factor ligand other than TNF α , wherein the fragment is a homolog of a cleavage site of native TNF α , and a Domain IV fragment of TNF α protein that binds to a TNF α receptor.
63. (New) A method for inducing apoptosis of a cell expressing a TNF α receptor, comprising introducing into the cell an encoding a chimeric TNF α polypeptide according to claim 52 wherein the chimeric TNF α polypeptide is expressed on the surface of the cell.
64. (New) A method for inducing activation of an immune system cell, comprising introducing into the cell a nucleic acid molecule encoding a chimeric TNF α polypeptide according to claim 52 wherein the chimeric TNF α polypeptide is expressed on the surface of the cell.
65. (New) A method for treating neoplasia in a patient comprising introducing into a neoplastic cell a nucleic acid molecule encoding a chimeric TNF α polypeptide according to claim 52 wherein the chimeric TNF α polypeptide is expressed on the surface of the cell.
66. (New) The method of claim 67 further comprising: obtaining the neoplastic cell from a human patient; infusing the neoplastic cell back into the patient after having introduced into the cells the nucleic acid molecule encoding the chimeric TNF α polypeptide.
67. (New) A method of treating neoplasia comprising directly injecting into a tumor bed of a patient the nucleic acid molecule encoding a chimeric TNF α according to claim 52 wherein the chimeric TNF α polypeptide is expressed in the tumor bed.

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62. (New) A chimeric TNFa ligand polypeptide, comprising a Domain III fragment of a tumor necrosis factor ligand other than TNFa, wherein the fragment is a homolog of a cleavage site of native TNFa, and a Domain IV fragment of TNFa protein that binds to a TNFa receptor.
63. (New) A method for inducing apoptosis of a cell expressing a TNFa receptor, comprising introducing into the cell an encoding a chimeric TNFa polypeptide according to claim 52 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
64. (New) A method for inducing activation of an immune system cell, comprising introducing into the cell a nucleic acid molecule encoding a chimeric TNFa polypeptide according to claim 52 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
65. (New) A method for treating neoplasia in a patient comprising introducing into a neoplastic cell a nucleic acid molecule encoding a chimeric TNFa polypeptide according to claim 52 wherein the chimeric TNFa polypeptide is expressed on the surface of the cell.
66. (New) The method of claim 65 further comprising: obtaining the neoplastic cell from a human patient; infusing the neoplastic cell back into the patient after having introduced into the cells the nucleic acid molecule encoding the chimeric TNFa polypeptide.
67. (New) A method of treating neoplasia comprising directly injecting into a tumor bed of a patient the nucleic acid molecule encoding a chimeric TNFa according to claim 52 wherein the chimeric TNFa polypeptide is expressed in the tumor bed.